

41. (Reiterated) The nucleic acid of claim 40, wherein one nucleic acid-binding domain includes a zinc finger motif and the other nucleic acid-binding domain includes a motif or domain selected from the group consisting of a helix-loop-helix motif, a helix-turn-helix motif, and a basic domain.

42. (Reiterated) The nucleic acid of claim 41, wherein the zinc finger motif is from a protein selected from the group consisting of transcription factor IIIA, SW15, Krüppel, Hunchback, and a steroid receptor.

43. (Reiterated) The nucleic acid of claim 41, wherein the zinc finger motif is from Zif268.

44. (Reiterated) The nucleic acid of claim 40, wherein one nucleic acid-binding domain includes a zinc finger motif and the other nucleic acid-binding domain includes a helix-turn-helix motif.

45. (Reiterated) The nucleic acid of claim 44, wherein the other nucleic acid-binding domain includes a homeodomain.

46. (Reiterated) The nucleic acid of claim 45, wherein the homeodomain is an Oct-1 homeodomain.

47. (Reiterated) The nucleic acid of claim 46, wherein the zinc finger motif is from a protein selected from the group consisting of transcription factor IIIA, Zif268, SW15, Krüppel, Hunchback, and a steroid receptor.

48. (Reiterated) The nucleic acid of claim 47, wherein the homeodomain is an Oct-1 homeodomain and the zinc finger motif is from Zif268.

49. (Amended) The nucleic acid of claim 48, wherein the chimeric protein further comprises a second zinc finger motif of Zif268.

50. (Reiterated) The nucleic acid of claim 49, which encodes ZFHD1.

51. (Reiterated) The nucleic acid of claim 41, wherein the other nucleic acid-binding domain is from a protein selected from the group consisting of Daughterless, Achaete-scute (T3), MyoD, and E12 E47.
52. (Reiterated) The nucleic acid of claim 41, wherein the other nucleic acid-binding domain is from a protein selected from the group consisting of MAT α 1, MAT α 2, MAT α 1, Antennapedia, Ultrabithorax, Engrailed, Paired, Fushi tarazu, HOX, Unc86, Oct 1, Oct2, and Pit.
53. (Reiterated) The nucleic acid of claim 41, wherein the other nucleic acid-binding domain is from a protein selected from the group consisting of GCN4, C/EBP, c-Fos, c-Jun, and JunB.
54. (Reiterated) The nucleic acid of claim 41, wherein the zinc finger motif is from a steroid receptor.
55. (Reiterated) The nucleic acid of claim 40, wherein the two nucleic acid-binding domains are separated by at least one amino acid.
56. (Reiterated) The nucleic acid of claim 40, wherein the chimeric protein binds with higher affinity to the composite binding site than to each of the portions of the composite binding site to which each of the two nucleic acid binding domains bind.
57. (Reiterated) The nucleic acid of claim 40, wherein the chimeric protein further comprises an additional domain.
58. (Reiterated) The nucleic acid of claim 57, wherein the additional domain is a regulatory domain.
59. (Reiterated) The nucleic acid of claim 58, wherein the regulatory domain is an activation domain.

60. (Reiterated) The nucleic acid of claim 59, wherein the activation domains is an Herpes Simplex Virus VP16 activation domain.

61. (Reiterated) The nucleic acid of claim 58, wherein the regulatory domain is a repression domain.

62. (Reiterated) The nucleic acid of claim 61, wherein the repression domains is from a Krüppel protein.

63. (Reiterated) The nucleic acid of claim 57, wherein the additional domain is a nucleic acid cleavage domain.

64. (Reiterated) The nucleic acid of claim 63, wherein the nucleic acid cleavage domain is the FokI cleavage domain.

65. (Reiterated) The nucleic acid of claim 57, wherein the additional domain is selected from the group consisting of a domain interacting with a cellular component, a domain which controls the stability of the chimeric protein, and a domain which controls subcellular localization.

66. (Amended) A nucleic acid encoding a chimeric protein which binds a nucleic acid comprising a composite binding site, wherein the chimeric protein comprises at least two nucleic acid-binding domains, each of which binds a sequence which is a portion of the composite binding site, wherein only one of the two nucleic acid-binding domains includes a DNA binding domain from a protein comprising a ~~homodomain~~ domain, and wherein the chimeric protein displays nucleic acid binding specificity that is distinct from the binding specificity of the individual nucleic acid-binding domains which comprise the chimeric protein.

67. (Reiterated) The nucleic acid of claim 66, wherein one nucleic acid-binding domain includes a helix-turn-helix motif and the other nucleic acid-binding domain includes a motif or domain selected from the group consisting of a zinc finger motif, a helix-loop-helix motif, and a basic domain.

68. (Reiterated) The nucleic acid of claim 66, wherein the chimeric protein further comprises an activation domain.
69. (Reiterated) The nucleic acid of claim 66, wherein the chimeric protein further comprises a repression domain.
70. (Reiterated) The nucleic acid of claim 66, wherein the chimeric protein further comprises an nucleic acid cleavage domain.
72. (Reiterated) A vector comprising a nucleic acid of claim 40.
73. (Reiterated) The vector of claim 72, further comprising expression control sequences permitting gene expression in eukaryotic cells.
74. (Amended) A kit comprising a vector of claim 72 and a gene operably linked to a composite binding site to which the chimeric protein encoded by the vector binds.
75. (Amended) A method for modulating expression of a gene in a cell, comprising expressing a chimeric protein in a cell which includes a gene operably linked to a composite binding site to which the chimeric protein binds, wherein the chimeric protein comprises two nucleic acid-binding domains, each of which binds a sequence which is a portion of the composite binding site, and wherein the chimeric protein displays nucleic acid binding specificity that is distinct from the binding specificity of the individual nucleic acid-binding domains which comprise the chimeric protein,
- whereby the chimeric protein binds the composite binding site, thereby modulating expression of the gene in the cell.
76. (Reiterated) The method of claim 75, wherein the chimeric protein further comprises an additional domain.

77. (Reiterated) The method of claim 76, wherein the additional domain is a regulatory domain.

78. (Reiterated) The method of claim 77, wherein the regulatory domain is an activation domain.

79. (Reiterated) The method of claim 78, wherein the activation domain is an Herpes Simplex Virus VP16 activation domain.

80. (Reiterated) The method of claim 77, wherein the regulatory domain is a repression domain.

81. (Reiterated) The method of claim 75, wherein one nucleic acid-binding domain includes a zinc finger motif and the other nucleic acid-binding domain includes a motif or domain selected from the group consisting of a basic domain, a helix-loop-helix motif, and a helix-turn-helix motif.

82. (Reiterated) The method of claim 81, wherein the other domain is a homeodomain.

83. (Reiterated) The method of claim 75, wherein the chimeric protein further comprises an additional nucleic acid-binding domain, which binds a sequence which is a portion of the composite binding site.

84. (Reiterated) The method of claim 83, wherein the additional nucleic acid-binding domain includes a zinc finger motif.

85. (Reiterated) A method for producing a cell for use in the method of claim 75, comprising introducing into a cell a nucleic acid encoding the chimeric protein.

86. (Reiterated) A method for producing a cell for use in the method of claim 75, comprising introducing into a cell a nucleic acid comprising a composite binding site.

87. (Reiterated) The method for claim 86, further comprising introducing into the cell a nucleic acid encoding the chimeric protein.

88. (Reiterated) The method of claim 87, wherein the gene encodes a recombinant gene product.

89. (Reiterated) The nucleic acid of claim 66, wherein one nucleic acid-binding domain includes a homeodomain.

90. (Reiterated) The nucleic acid of claim 40, further comprising an additional nucleic acid-binding domain, which binds a sequence which is a portion of the composite binding site.

91. (Reiterated) The nucleic acid of claim 66, further comprising an additional nucleic acid-binding domain, which binds a sequence which is a portion of the composite binding site.

92. (Reiterated) The nucleic acid of claim 71 further comprising an additional nucleic acid-binding domain, which binds a sequence which is a portion of the composite binding site.

93. (Reiterated) The nucleic acid of claim 75, further comprising an additional nucleic acid-binding domain, which binds a sequence which is a portion of the composite binding site.

94. (Reiterated) The nucleic acid of claim 57, wherein the additional domain is heterologous with respect to the two nucleic acid-binding domain.

95. (Reiterated) The nucleic acid of claim 68, wherein the activation domain is heterologous with respect to the two nucleic acid-binding domains.

96. (Reiterated) The method of claim 76, wherein the additional domain is heterologous with respect to the two nucleic acid-binding domains.

97. **(Reiterated)** The nucleic acid of claim 40, which encodes a chimeric protein which binds the composite binding site that is not a naturally-occurring binding site of a naturally-occurring transcription factor.

98. **(Reiterated)** The nucleic acid of claim 66, which encodes a chimeric protein which binds the composite binding site that is not a naturally-occurring binding site of a naturally-occurring transcription factor.

The claims presented above incorporate changes as indicated by the marked-up version below.

40. **(Thrice Amended)** A nucleic acid encoding a chimeric protein which binds a nucleic acid comprising a composite binding site, wherein the chimeric protein comprises two nucleic acid-binding domains, each of which binds a sequence which is a portion of the composite binding site, wherein only one of the two nucleic acid-binding domains includes zinc finger motif, and wherein the chimeric protein displays nucleic acid binding specificity that is distinct from the binding specificity of the individual nucleic acid-binding domains which comprise the chimeric protein two nucleic acid-binding domains

- (i) — do not occur in the same protein in nature;
- (ii) — do not occur in the same protein in nature in the order in which they are present in the chimeric protein; or
- (iii) — do not occur in nature with the same spacing that is present in the chimeric protein.

49. **(Amended)** The nucleic acid of claim 48, wherein the chimeric protein further comprises a second zinc finger motif of Zif268.

66. **(Amended)** A nucleic acid encoding a chimeric protein which binds a nucleic acid comprising a composite binding site, wherein the chimeric protein comprises at least two nucleic acid-binding domains, each of which binds a sequence which is a portion of the composite binding site, wherein only one of the two nucleic acid-binding domains includes a DNA binding

domain from a protein comprising a homeodomain, and wherein the chimeric protein displays nucleic acid binding specificity that is distinct from the binding specificity of the individual nucleic acid-binding domains which comprise the chimeric protein which nucleic acid binding domains

- (i) — do not occur in the same protein in nature;
- (ii) — do not occur in the same protein in nature in the order in which they are present in the chimeric protein; and/or
- (iii) — do not occur in nature with the same spacing that is present in the chimeric protein.

74. (Amended) A kit comprising a vector nucleic acid of claim 72 and a gene operably linked to a composite binding site to which the chimeric protein encoded by the vector binds.

75. (Amended) A method for modulating expression of a gene in a cell, comprising expressing a chimeric protein in a cell which includes a gene operably linked to a composite binding site to which the chimeric protein binds, wherein the chimeric protein comprises two nucleic acid-binding domains, each of which binds a sequence which is a portion of the composite binding site, and wherein the chimeric protein displays nucleic acid binding specificity that is distinct from the binding specificity of the individual nucleic acid-binding domains which comprise the chimeric protein which nucleic acid binding domains

- (i) — do not occur in the same protein in nature;
- (ii) — do not occur in the same protein in nature in the order in which they are present in the chimeric protein; and/or
- (iii) — do not occur in nature with the same spacing that is present in the chimeric protein,

whereby the chimeric protein binds the composite binding site, thereby modulating expression of the gene in the cell.